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Retinal Function: Coupling Cones Clarifies Vision

Dispatch

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Gap junctions have been shown to electrically couple cone photoreceptors: coupling blurs the image coded by cones, but this loss is offset by a decrease in noise. Electrical coupling thus improves the resolution of signals distributed across groups of cells.

The quality of the signals in our photoreceptors limits what we can and cannot see. Take two-point resolution. To tell that a distant bright speck is two thin polar bears, rather than one fat one, two conditions must be met. At least three photoreceptors must be involved: one for each of the bears, and a third to show the space between them. To see the gap, the signal in the middle photoreceptor must be noticeably different from its two neighbors' (Figure 1). It follows that our two-point resolution is limited by the spacing of our narrowest and most densely packed photoreceptors — our foveal cones. Anything that reduces the difference between the signals in neigh-boring cones reduces our ability to resolve two points. A familiar culprit is optical blur, which spreads light from a single point across several cones (Figure 1). It was surprising, therefore, to see gap junctions connecting cones in electron micrographs [1]. Gap junctions electrically couple cells, for example at electrical synapses, and will therefore impair spatial resolution by reducing the differences between signals in neighboring cones (Figure 1).

A joint study by three groups [2], published recently in *Current Biology*, has now resolved the paradox of cone gap junctions. Electrical coupling turns out to improve spatial resolution by reducing noise. The combined approaches taken by the three groups — physiology, psychophysics and modelling — provide a compelling account of the function of this neural interaction by answering three questions. How strongly do gap junctions electrically couple cones? Does coupling affect the performance of the intact cone array? And does coupling improve vision?

In this new work, the strength of electrical coupling was measured directly, by making whole cell recordings from pairs of cones in slices of ground squirrel retina, injecting current into one cell and recording the response of the other. Electrical coupling was found to be significant, and to be unaffected by neuromodulators that change the properties of other retinal circuits.

Sophisticated psychophysical tests showed that cones in the intact human retina behave as if they are coupled [2]. Electrical coupling will reduce acuity by distributing the signal from a single point to several cones. But because this coupling effect is superimposed on the broader optical point spread function of the eye's focusing system (Figure 1), it is difficult to detect the influence of cone coupling on human visual acuity. By steering coherent monochromatic laser light through a subject's pupil, one can form an interference pattern of regular stripes directly on their cone array [3]. The stripe width can be varied to values less than the diameter of a single cone to measure visual acuity.

The psychophysicists among DeVries *et al.* [2] exploited a clever trick that can be used to isolate the spatial sensitivity of cones from the effects of neural interactions higher up in the visual system [4]. When two fine interference patterns are superimposed on a subject's cone array, he or she sees a coarser pattern, which is a distortion product produced by non-linearities in the nervous system. By varying the width of the fine laser patterns and measuring the changes in the

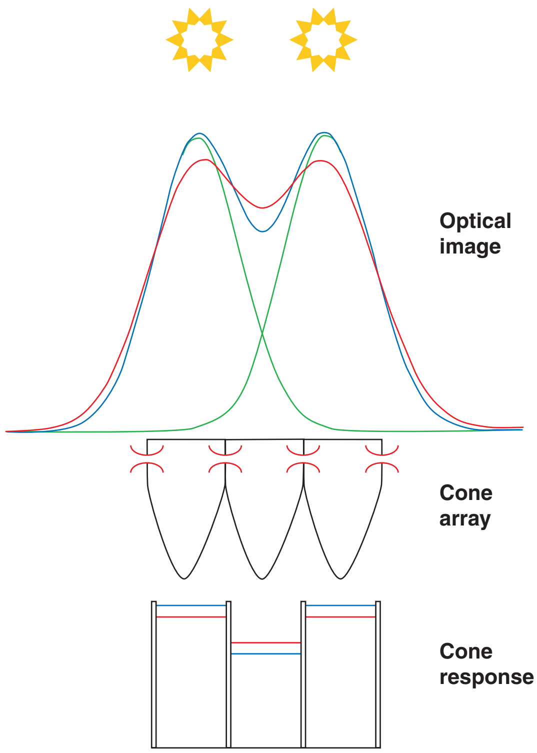

Figure 1. Cone coupling and spatial resolution.

The light from two points is blurred by the optical point spread function of the eye's optics (green), so that the resulting image (blue) is two broad peaks separated by a shallow dip. Three cones are required to resolve the two points, one for each peak and one for the dip. The dip must be deep enough to produce a signal in the central cone that is detectably different from its neighbors. Gap junctions and their effects are shown in red. Gap junctions reduce the difference between signals in neighboring cones by electrical coupling. Their effect is equivalent to a small increase in the width of the optical image and a decrease in its depth.

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visibility of the coarser distortion product, the psychophysicists deduced the spatial sensitivity of foveal cones. This fine technique showed that the central peak in cone sensitivity, corresponding to light entering a single cone, is surrounded by a ring, corresponding to signals from electrically coupled neighbors [2]. The spatial sensitivity of cones is unaffected by changes in light level, suggesting again that coupling is not modulated.

DeVries *et al.* [2] went on to formulate an electrical model of the cone array, which shows that coupling improves vision by reducing the noise level. If signals from neighboring cones are added, the noise produced by photons and ion channels tends to cancel out [5,6]. With less noise, one can resolve smaller differences in cone signal. For all but the tiniest stimuli, this improvement in resolution more than compensates for the reduction in signal differences caused by coupling. Thus cone coupling clarifies vision by judiciously blurring the image.

The electrical coupling of cones is good neural engineering. Gap junctions are simple, cheap and reliable, and the alternative fast mechanism — a chemical synapse — would inject noise into a noise reduction network. Electrical synapses are found in other networks where reliability and precision are important, including invertebrate photoreceptors [7], auditory and electrosensory systems [8], motor pattern generating circuits [9], and networks of neurons deeper in the retina [10]. But, if neurons deeper in the retina are coupled, why couple cones?

Spatial detail destroyed by cone coupling cannot be recovered later in visual processing. In principle, the eye could keep cones separate to preserve spatial detail, and reduce noise later by coupling neurons. But there are good reasons to couple cells before they synapse [6,7]. Reducing noise levels before transmission reduces the risk of saturating the synapse. Coupling also prevents synaptic non-linearities from disrupting noise reduction. Recall that coupling reduces noise by cancelling positive and negative fluctuations in neighboring cells. The non-linear input–output function of a chemical synapse skews these fluctuations by amplifying inputs of different amplitude by different amounts, and this skew invalidates the cancellation of noise [2].

The simplicity of electrical coupling should not blind us to its many advantages. In development, gap junctions could clarify the spatial distribution of morphogenetic signals to make patterning more reliable. Note here that, just as cones drive non-linear synapses, morphogens drive non-linear 'either/or' decisions of cell fate. Nor should we underestimate the role of electrical synapses in neural computation. In the salamander retina, an electrically coupled network of voltage sensitive rod inner segments can pick out the advancing edges of approaching prey [11]. Few circuit designers would choose to dispense with the electronic equivalent of electrical coupling — the resistor.

The remarkably complete analysis by DeVries *et al.* [2] of a relatively simple interaction, cone coupling, demonstrates the power of combining anatomy, physiology, psychophysics and modelling in studies of retina. Neuroanatomists reconstruct retinal circuits and identify both the sites of signaling, and their molecular mechanisms [12,13]. Physiologists use whole cell recordings to describe how these circuits process signals [2,14]. Psychophysicists have sophisticated optical systems [2,15] that can microstimulate intact retina and establish the action of circuits. Computational neuroscientists apply the powerful models that are appropriate for the level of complexity found in retina [2]. Add more attention to natural stimuli [16] and to behavior [17], and we have a potent combination. We can expect more analyses that are sufficiently complete to establish function and discover general principles of cell signaling and information processing.

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